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Associations Between Birth Weight, Obesity, Fat Mass and Lean Mass in Korean Adolescents: The Fifth Korea National Health and Nutrition Examination Survey

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SCHOLARONE™ Manuscripts Associations Between Birth Weight, Obesity, Fat Mass and Lean Mass in Korean Adolescents: The Fifth Korea National Health and Nutrition Examination Survey

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ABSTRACT

Objective

Previous studies on the relation between birth weight and obesity in adolescents had inconsistent results. Moreover, few studies targeted Asian adolescents although there are ethnic differences in programming of body composition. This inconsistency and lack of studies in body composition of Asians make it necessary for further study. Therefore, this study aimed to investigate the association between birth weight, obesity, fat mass and lean mass in Korean adolescents.

Methods

This study was a cross-sectional analysis and participants were 1,304 people (693 men and 611 women) aged 12-18. Among participants in the KNHANES V (n=1,510), we excluded participants who did not respond to the birth weight questionnaire and those who did not have BMI information. For body composition study, only those with DXA examination (n=884) were used among the study population.

Multivariable logistic regression and least square means were used. Sociodemographic factors, health behaviors, health status and gestational age were adjusted.

Results

Individuals with highest 20% birth weight were more likely to be overweight (aOR=1.86; 95% CI=1.02-3.50) than those with normal birth weight. Women who had highest 20% birth weight were more likely to have obesity (aOR=3.85; 95% CI=1.31-11.29). Those with highest 20% birth weight had higher FMI and LMI (P value: 0.06, 0.19) after adjustment. Only FMI but not LMI tend to increase with birth weight in female population (P for trend: <0.01, 0.10).

Conclusions

Our study suggests that high birth weight could be an indicator of obesity, with more tendency in increasing fat mass than lean mass, especially in women.

Keywords: Birth weight · Obesity · Body composition · KNHANES V

Strengths and limitations of this study

- We used large study population (n=1,304) compared to previous studies, which hardly exceed 100
 people, and used the data of Asians, whom few previous studies targeted.
- This study considered not only relations between birth weight and BMI, but also specific body compositions including fat mass and lean mass.
- There was no preceding research that adjusted as many related variables as we did, which raises credibility of this study.
- Since cross-sectional data are used, inferences about causal effects cannot be made and only
 assumptions about the relation can be suggested.
- Birth weight and other controlled variables were self-reported in the survey used in this study, which may had made recall bias.

INTRODUCTION

Prevalence of obesity in adolescents has been increasing worldwide and is of great concern. Since obesity in earlier life is tightly correlated with adult diseases[1,2], clarifying its risk factors and prevention remain an important goal. Among various risk factors of obesity, early life events have been suggested to play an important role, by lasting changes in body composition and appetite control by central nervous system[3]. Also, one's ability to regulate and metabolize food throughout life is known to be determined pre or postnatally[4].

Birth weight, among those early life factors, is an important topic that claims our attention, as it is closely related to factors such as intrauterine nutrition[5] and early body composition. Previous studies demonstrated that birth weight is associated with obesity in adults. Many of the studies showed that high birth weight increases the risk of obesity in adults[3,6,7] and some added that low birth weight reduces it[3].

However, studies about the relation between birth weight and obesity in adolescents had inconsistent results. Some insisted that there are J-shaped relationships or linear relationships between birth weight and BMI in childhood[8-10]. Others showed no significant relationship[11]. Meanwhile, previous studies about the relationship between birth weight and body composition showed that birth weight is more related to lean mass compared to fat mass in United Kingdom adolescents[12,13], and in Brazilian 9 years children[14]. However, although there are ethnic differences in programming of body composition[15,16], few studies targeted Asian adolescents.

This inconsistency among the studies of obesity and lack of studies in body composition of Asians make it necessary for further study. Thus we focused on re-evaluating gender-specific association between birth weight and body composition including BMI in adolescents, using the data from the fifth Korean National Health and Nutrition Examination Survey of 2010-2011 (KNHANES V).

METHODS

Study population and data collection

This study used the fifth KNHANES, a national survey that represents the Korean population. KNHANES V contains health interview survey, health behavior survey, health examination survey and nutrition survey. It was organized by Korean Ministry of Health and Welfare from 2010 to 2011. Target sampling follows a stratified multi-stage clustered probability design.

Those aged from 12 to 18 among the participants in the KNHANES V (n=1,510) were initially selected for this study. First, we excluded participants who did not respond to the birth weight questionnaire (n=203). Second, among this population (n=1,307), those who did not have BMI information were excluded (n=3). The final study population included 1,304 individuals (693 men and 611 women) for obesity study (Figure 1). For body composition study, only those with DXA examination (n=884) were used among the study population.

Sociodemographic, biomedical and lifestyle factors

This study considered several factors that could affect outcome of the analyses. First of all, sociodemographic variables including age, sex, residential area, and household income were self-reported by the participants. Residential area was categorized into capital city, metropolitan area, and town/city. As the study population was adolescents who usually have no income, household income was considered instead of personal income. Household income was categorized into three levels. Second, we also used the information on various health behaviors (smoking, drinking, physical activity, energy consumption, sleep duration). We categorized participants into two groups regarding unhealthy behaviors: those who had experienced smoking or drinking at least once, and those who had not. Other variables were adjusted as continuous variables. For physical activity, this study used the level of physical activity suggested by the International Physical Activity Questionnaire (IPAQ)[17] calculating Metabolic Equivalent Task (MET) per week. Third, health status related to obesity was also considered. Participants were divided into two groups regarding comorbidities: those with at least one comorbidity (hypertension, diabetes, asthma, impaired fasting glucose), and those without any. Diabetes and asthma were diagnosed by doctors. As participants were adolescents, those with blood pressure higher than 90% of their age and sex were classified as having hypertension. Those with fasting blood sugar higher than 100 mg/dL were classified as having impaired fasting glucose. Finally, participants were divided into three groups according to their gestational age: preterm (\leq 36 weeks), normal and postterm (\geq 42 weeks).

Assessment of birth weight, body composition and obesity

Birth weight was reported by participants' mothers in KNHANES V. We categorized participants into five groups according to their percentile of birth weight. Cutoff points for each group were 2.89kg, 3.19kg, 3.3kg, 3.62kg. The group in the middle (40~60%, birth weight between 3.19kg and 3.3kg) was used as the reference.

In KNHANES V, body compositions were measured by skillful technicians, providing accurate and reliable data. All the participants were changed into light clothing with all jewelry removed, and then experienced DXA for estimation of body composition. Body Mass Index (BMI) was calculated by dividing weight by height squared (kg/m²). Total fat mass and lean mass provided from DXA were converted in the same way in this study. We divided total fat mass and lean mass by height squared to calculate Fat Mass Index (FMI) and Lean Mass Index (LMI) (kg/m²).

Considering the ethnic differences, we used definition of obesity for Asians proposed by the World Health Organization Western Pacific Region[18], which slightly differed from that for Westerns. We classified the study participants into overweight (BMI \geq 85 percentile BMI of age and sex or 23 kg/m², but not obesity) and general obesity (BMI \geq 95 percentile BMI of age and sex or 25 kg/m²).

Statistical analysis

All statistical analysis was done by utilizing Stata 13.0 (STATA Corp., College Station, TX, USA). In this study, we used multivariable logistic regression in order to calculate the adjusted odds ratio (aOR) and 95% confidence intervals (95% CI) of overweight and general obesity according to birth weight. Sociodemographic factors, health behaviors, health status and gestational age were adjusted. For the study population to represent the entire adolescents of the nation, we took complex sampling design into account by using the estimation command "svy" before statistical analysis. Next, we used least squares means adjusted for the same factors to examine the association between birth weight and body composition for the total study population, men, and women. Based on a multiple linear regression, the linear trend of adjusted means for FMI and LMI was tested across birth weight.

RESULTS

Characteristics of the study population

General characteristics of the total study population, male participants, and female participants are shown in Table 1. In total population, mean birth weight was 3.3kg, and was slightly higher in men than women. Among study population, prevalence of overweight and obesity was higher in men than women. Mean(SD) FMI in adolescence was $5.8 \ (\pm 2.5) \ kg/m^2$ in total population, $5.0 \ (\pm 2.5) \ kg/m^2$ in men and $6.7 \ (\pm 2.2) \ kg/m^2$ in women. Mean(SD) LMI was $15.0 \ (\pm 2.1) \ kg/m^2$ in total population, $16.0 \ (\pm 2.0) \ kg/m^2$ in men, and $13.8 \ (\pm 1.5) \ kg/m^2$ in women.

Relationship between birth weight, overweight and obesity

Table 2 shows total and sex-stratified odds ratio of overweight and general obesity according to birth weight. In both sexes, unadjusted OR for overweight in the high birth weight group (highest 20% group) was 2.02 (95% CI=1.11-3.68) compared to the reference group. In the adjusted analysis, high birth weight group also had higher odds of being overweight (aOR=1.86; 95% CI=1.02-3.50) compared to the reference group. In male population, unadjusted OR for overweight was 3.09 (95% CI=1.41-6.75), and the association remained after adjustment (aOR=2.86, 95% CI=1.12-7.31). However, there was no association between high birth weight and obesity in men (aOR=0.77, 95% CI=0.34-1.76). In contrast, in women, adjusted analysis demonstrated the association between high birth weight and general obesity after adjustment (aOR=3.85; 95% CI=1.31-11.29), but no association with overweight. (aOR: 1.04, 95% CI=0.39-2.78).

Relationship between birth weight and body composition

The association between birth weight, fat mass, and lean mass of total participants is presented in Figure 2. Result of female participants is presented in Figure 3 and that of male participants is presented in Figure 4. After adjusting sociodemographic factors, health behaviors, health status and gestational age, least squares means of FMI and LMI both increased significantly with higher birth weight in total population (*P* for trend <0.01, 0.02). High birth weight group (Highest 20%) had higher FMI and LMI than the reference group (P value: 0.06, 0.19 respectively). In male participants, higher birth weight was associated with higher FMI and LMI (P for trend: 0.05, 0.22). In female participants, higher birth weight was also associated with higher FMI (P for trend: 0.01), but LMI showed an inverse U-shape (P for trend: 0.10). Both high birth weight group and low birth weight group had lower lean mass compared to the reference group (P value: 0.45, 0.01, respectively) in female adolescents.

Table 1. General characteristics of the study population

	Total (n=1,304)	Men (n=693)	Women (n=611)
Age (year), mean±s.d	14.7 (2.0)	14.7 (2.0)	14.8 (1.9)
Residence			
Capital	284 (21.8)	151 (21.8)	133 (21.8)
Metropolitan	279 (21.4)	148 (21.4)	131 (21.4)
Town/City	741 (56.8)	394 (56.9)	347 (56.8)
Household Income			
Lowest Third	144 (11.2)	64 (9.4)	80 (13.3)
Middle Third	727 (56.6)	385 (56.5)	342 (56.8)
Highest Third	413 (32.2)	233 (34.2)	180 (29.9)
Physical Activity(MET-min) a, mean±s.d	2376.7 (2964.7)	2839.4 (3164.5)	1849.8 (2624.3)
Unhealthy Behaviors	342 (26.2)	201 (29.0)	141 (23.1)
Sleep Duration, mean±s.d	7.2 (1.4)	7.2 (1.3)	7.1 (1.5)
Total Energy Intake/day(kcal), mean±s.d	2252.1 (915.0)	2521.4 (959.4)	1952.8 (758.9)
Comorbidity	240 (18.4)	143 (20.6)	97 (15.9)
Gestational Age(week)			
Preterm (≤36)	47 (3.6)	20 (2.9)	27 (4.4)
Normal (37~41)	1,211 (93.1)	656 (94.8)	555 (91.1)
Postterm (≥42)	43 (3.6)	16 (2.3)	27 (4.4)
Birth Weight, mean±s.d	3.3 (0.5)	3.3 (0.5)	3.2 (0.5)
Obesity			
Overweight b	162 (12.4)	97 (14.0)	65 (10.6)
General Obesity ^c	171 (13.1)	102 (14.7)	69 (11.3)
Body Composition			
Body Mass Index (kg/m ²), mean±s.d	21.0 (3.7)	21.2 (3.8)	20.7 (3.4)
Fat Mass Index (kg/m ²), mean±s.d	5.8 (2.5)	5.0 (2.5)	6.7 (2.2)
Lean Mass Index (kg/ m ²), mean±s.d	15.0 (2.1)	16.0 (2.0)	13.8 (1.5)

Note: Data presented in number (percentage) with appropriate units unless otherwise stated.

^a Metabolic Equivalent Task based on the International Physical Activity Questionnaire(IPAQ).

^b Overweight: BMI ≥ 85 percentile BMI of age and sex or 23 kg/m², but not obesity

^c General Obesity (Korean criteria): BMI \geq 95 percentile BMI of age and sex or 25 kg/m²

Table 2: Crude and adjusted analyses of the association between birth weight and obesity in Korean adolescents

	Overweight Gene			General Ob	General Obesity		
Birth Weight	Proportion n (%)	Crude OR (95% CI)	Adjusted ^a OR (95% CI)	Proportion n (%)	Crude OR (95% CI)	Adjusted ^a OR (95% CI)	
0-20 percentile							
Men (n=101)	13 (12.9)	1.73 (0.68-4.39)	1.58 (0.55-4.53)	14 (13.9)	0.83 (0.34-2.03)	0.74 (0.27-2.01)	
Women (n=134)	10 (7.5)	0.52 (0.20-1.37)	0.84 (0.30-2.37)	14 (10.5)	1.26 (0.50-3.20)	1.55 (0.47-5.11)	
Total (n=235)	23 (9.8)	0.97 (0.49-1.91)	1.17 (0.54-2.52)	28 (11.9)	0.96 (0.51-1.81)	1.02 (0.49-2.13)	
20-40 percentile							
Men (n=135)	15 (11.1)	1.33 (0.53-3.36)	1.92 (0.66-5.53)	17 (12.6)	0.72 (0.32-1.62)	0.73 (0.30-1.79)	
Women (n=136)	14 (10.3)	0.81 (0.32-2.07)	0.65 (0.25-1.69)	15 (11.0)	1.83 (0.70-4.78)	2.53 (0.85-7.55)	
Total (n=271)	29 (10.7)	1.04 (0.54-2.01)	1.08 (0.52-2.26)	32 (11.8)	1.09 (0.59-2.04)	1.19 (0.62-2.27)	
40-60 percentile							
Men (n=145)	14 (9.7)			23 (15.9)			
Women (n=138)	14 (10.1)	1 (referent)	1 (referent)	13 (9.4)	1 (referent)	1 (referent)	
Total (n=283)	28 (9.9)			36 (12.7)			
60-80 percentile							
Men (n=149)	25 (16.8)	1.75 (0.79-3.86)	2.39 (0.94-6.12)	19 (12.8)	0.88 (0.39-1.99)	0.56 (0.23-1.37)	
Women (n=109)	15 (13.8)	1.15 (0.47-2.84)	1.19 (0.43-3.28)	13 (11.9)	1.74 (0.68-4.47)	2.61 (0.85-7.99)	
Total (n=258)	40 (15.5)	1.44 (0.80-2.59)	1.61 (0.82-3.18)	32 (12.4)	1.18 (0.64-2.18)	1.03 (0.52-2.02)	
80-100 percentile							
Men (n=163)	30 (18.4)	3.09 (1.41-6.75)	2.86 (1.12-7.31)	29 (17.8)	1.01 (0.49-2.05)	0.77 (0.34-1.76)	
Women (n=94)	12 (12.8)	0.82 (0.31-2.14)	1.04 (0.39-2.78)	14 (14.9)	2.18 (0.86-5.55)	3.85 (1.31-11.29)	
Total (n=257)	42 (16.3)	2.02 (1.11-3.68)	1.86 (1.02-3.50)	43 (16.7)	1.39 (0.79-2.44)	1.50 (0.80-2.81)	
P for trend							
Men		0.08	0.15		0.53	0.83	
Women		0.19	0.34		0.38	0.18	
Total		0.02	0.10		0.24	0.44	

Acronyms: OR, Odds Ratio; CI, Confidence Intervals

P for trend: P for trend for adjusted analyses

^{*}Adjusted for age, sex, residence, household income, physical activity, total energy intake, sleep duration, unhealthy behaviors, comorbidities and gestational

DISCUSSION

In this cross-sectional study of 12 to 18 years old Korean adolescents, we found association between birth weight and overweight in males, and obesity in females. Also, higher birth weight was related to both higher LMI and FMI, with more tendency in FMI. Sex difference was shown in both analyses. Prevalence of adolescents' obesity in Korea increased from 6.8% in 1998 to around 10% in 2005[19,20], and was 13.1% in the data used in this study. This fast increase may be attributed to economic development and westernization of diets in Korea. Obesity in adolescence not only causes diseases such as cardiovascular diseases, pulmonary diseases, but also has psychosocial consequences[21], which could have long lasting effects. This makes prevention and care of adolescence obesity an important issue.

Higher birth weight was associated with increased prevalence of overweight in total population and in male adolescents in this study. This result is consistent with the previous cohort studies that showed birth weight is associated with overweight in male adolescents[11,22]. Meta-analysis on birth weight and long-term overweight risk is also consistent with our study that later overweight is associated with high birth weight[23].

High birth weight did increase the risk of obesity in female population, but not in total population or male population. This result differs from previous studies that have shown that high birth weight increases the risk of obesity in adolescents[8,10]. However, it was consistent with the study[11] that have additionally adjusted for more possible cofounders including physical activity and family income. Our study adjusted for the biggest number of cofounders including sleep duration, unhealthy behaviors and comorbidities, which could be the reason for the difference. There are also many studies that have shown the relationship between birth weight and overweight/obesity in children[8,24], and in adults[3,6,7]. The reason for the difference here could be the effect of maturation in adolescence. It is known that alterations in body fat distribution begins during puberty, due to hormones including cortisol, insulin, growth hormone, and the sex steroids[25]. The fact that adolescents are in the middle of these changes that occur during maturation may have caused the difference of results with adults or children.

Using the body composition data by DXA, this study found that higher birth weight was related to higher LMI. This is consistent with preceding studies which insisted that birth weight is associated with later lean mass[12-14]. In addition to this, we found the association between higher birth weight and higher FMI with significant tendency. One possible explanation for this trend in increasing fat mass in Korean adolescents may be ethnic differences. It is known that BMI and body fat percent is ethnic specific, possibly due to differences in

frame size, relative leg length and physical activity level[15,26]. It is also said that Asians usually have more fat but lower BMI compared to whites[16].

For the association between birth weight, obesity, FMI and LMI shown in this study, common genetic factors may be one possible explanation. It is said that about 50% of the variance in birth weight and more than that of the variance in BMI are attributed to shared genetic factors[27,28]. Therefore, it seems rational to speculate that the factors that made infants heavy could also increase the risk of higher BMI in later life. Another explanation could be that intrauterine environment, which obviously determines birth weight, also affects formation of the fetal organs involved in energy metabolism by altering the transfer of metabolic substances between mother and fetus[29].

In this study, relation between birth weight and both obesity and body composition showed gender differences. Among studies that dealt relationships between birth weight and possible outcomes in later life including obesity, blood pressure[30], lipid levels[31] and insulin action[32], many have shown gender differences. These findings indicate that males and females could have different mechanism of programming in early life. Although exact mechanism for this difference has not been explained, we suggest several explanations. It is suggested that sex steroid hormones affect in programming body composition during pubertal development[33,34]. Estrogen, for example, is known to play an important role in body fat distribution[33]. This difference in hormone actions lead to more increased lean mass in boys, and comparatively high fat mass in girls[35]. Moreover, some studies suggested that bone and muscle growth may be programmed differently by gender during intrauterine life[36,37]. These factors may have contributed to stronger tendency in results in female.

High BMI may not be the perfect measure of obesity, as it does not contain information about fat distribution[38]. To supplement this limitation, this study also considered FMI and LMI in addition to BMI. High BMI with high FMI but not LMI, is indeed dangerous, with potential risk of leading to other diseases by dropping the level of immunity. As our study showed that high birth weight is associated with overweight and obesity, with higher FMI than LMI especially in female, those born with high weight should be taken care of. If infants are born with high weight, early intervention would be needed against obesity by managing diet and physical activity level since young.

There are several limitations in this study. First of all, since cross-sectional data are used, inferences about causal effects cannot be made and only assumptions about the relation can be suggested. Longitudinal studies are needed to clarify if birth weight have effects on later obesity and body composition. Secondly, birth

weight was self-reported in the survey used in this study, which means that the data could be less accurate compared to birth records. Other controlled variables including sleep duration, physical activity were also selfreported, which may had made recall bias. Although parental factors including maternal obesity, diabetes influence their offspring, they are not considered in this study since KHANES V did not include such topics in the survey. Despite these limitations, our study has strength that we used large study population (n=1,304) compared to previous studies, which hardly exceed 100 people. We also tried to supplement missing parental factors by adjusting household income in the analysis. Moreover, as far as we know, there were no preceding research that adjusted as many related variables as we did, which raises credibility of this study. Most importantly, this study filled up the lack of study among Asians and inconsistency that existed in previous studies, suggesting that ethnic differences and gender differences may exist in programming of body resity. composition and obesity.

CONCLUSION

The results of our study suggest that high birth weight may be an indicator of overweight in Korean adolescents. Especially in women, high birth weight is associated with general obesity. Difference in fat mass was more significant than lean mass between those with high and normal birth weight. Especially in women, only fat mass showed an increasing trend across birth weight. These findings suggest that those born with high birth weight, especially females, need early intervention against obesity.



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CONTRIBUTORSHIP

In this study, Myunggee Kang designed the study, analyzed the data, interpreted the results and wrote the paper as a first author. Jung Eun Yoo contributed to data analysis and result interpretation. Kyuwoong Kim contributed to data analysis and literature research. Sang Min Park contributed to study design and results interpretation. All authors were involved in revising the paper and approved the final paper as submitted.

CONFLICT OF INTEREST STATEMENT

No conflict of interest was declared.

ETHICAL APPROVAL

This study did not need ethical approval of our Institutional Review Board, since the survey data examined were publicly available.

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DATA SHARING

All relevant materials are provided in the manuscript. KNHANES V, raw data used in this is available from $\underline{\text{http://knhanes.cdc.go.kr.}}$

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Figure 1: Flow Diagram of the Selection Procedure for the Study Population

Figure 2: Least-squares means of FMI and LMI in total participants (n=884). We adjusted for socioeconomic, health status, health behavior factors according to birth weight.

Figure 3: Least-squares means of FMI and LMI in female participants (n=407). We adjusted for socioeconomic, health status, health behavior factors according to birth weight.

Figure 4: Least-squares means of FMI and LMI in male participants (n=477). We adjusted for socioeconomic, health status, health behavior factors according to birth weight.



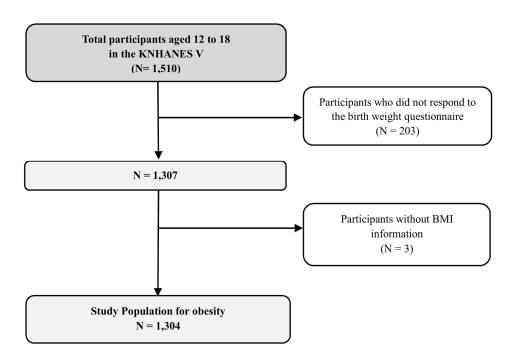


Figure 1: Flow Diagram of the Selection Procedure for the Study Population $87x59mm (600 \times 600 DPI)$

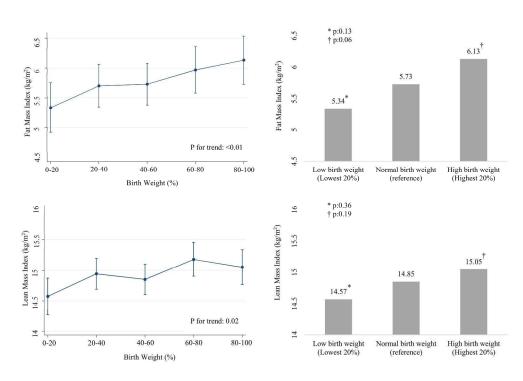


Figure 2: Least-squares means of FMI and LMI in total participants (n=884). We adjusted for socioeconomic, health status, health behavior factors according to birth weight.

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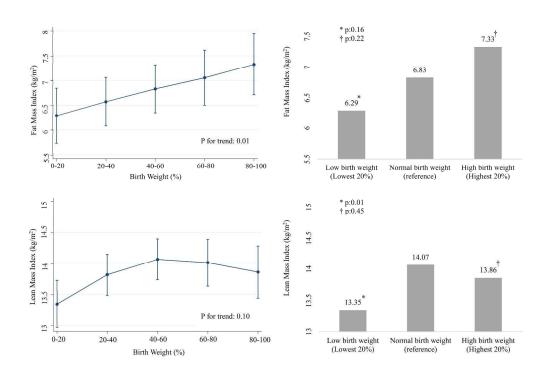
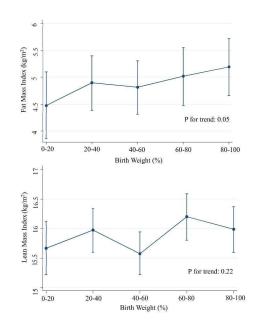


Figure 3: Least-squares means of FMI and LMI in female participants (n=407). We adjusted for socioeconomic, health status, health behavior factors according to birth weight.

144x99mm (600 x 600 DPI)



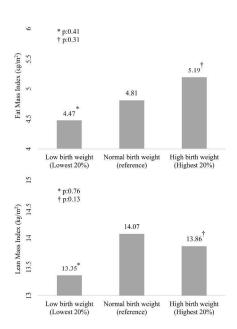


Figure 4: Least-squares means of FMI and LMI in male participants (n=477). We adjusted for socioeconomic, health status, health behavior factors according to birth weight.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	Data removed
		(d) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	5
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8
		(b) Indicate number of participants with missing data for each variable of interest	5
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(b) Report category boundaries when continuous variables were categorized	5,6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11,12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10,11
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Associations Between Birth Weight, Obesity, Fat Mass and Lean Mass in Korean Adolescents: The Fifth Korea National Health and Nutrition Examination Survey

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SCHOLARONE™ Manuscripts Associations Between Birth Weight, Obesity, Fat Mass and Lean Mass in Korean Adolescents: The Fifth Korea National Health and Nutrition Examination Survey

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ABSTRACT

Objective

Previous studies on the relationship between birth weight and obesity in adolescents have been

inconsistent and mostly targeted adolescents in Western countries. Therefore, we aimed to investigate the

association between birth weight, obesity, fat mass and lean mass in Korean adolescents using the fifth Korea

National Health and Nutritional Examination Survey (KNHANES V).

Methods

Among participants aged between 12 and 18 years in the KNHANES V (n=1,510), we excluded

participants who did not respond to the birth weight questionnaire and those who did not have BMI values,

resulting in a study population of 1,304 (693 men and 611 women) people. For the body composition study, only

those who underwent DXA examinations (n=884) were used among the study population.

Multivariable logistic regression was used to examine the relationship between birth weight and

obesity. Least square means were used to study birth weight and body composition. Sensitivity analysis was

performed additionally.

Results

Individuals within the highest 25th percentile in birth weight were more likely to be overweight

(adjusted odds ratio, aOR=1.64, 95% confidence interval, CI=1.05-2.57) than those with normal birth weight.

Women who were in the highest 25th percentile in birth weight were more likely to be obese (aOR=2.15, 95%

CI=1.06-4.37). Fat mass index (FMI), but not lean mass index (LMI), significantly increased with increasing

birth weight. (P for trend: 0.03). This tendency remained in female population (P for trend: 0.03).

Conclusions

High birth weight could be a predictor of obesity, with greater birth weight leading to increasing fat

mass, but not lean mass. These findings suggest that those born with high birth weight may merit close

monitoring and early intervention against obesity.

Keywords: Birth weight · Obesity · Body composition · KNHANES V

Strengths and limitations of this study

- The study population of this study consisted of Koreans, an ethnicity few previous studies targeted, and was relatively large (1,304 people), raising the credibility of this study.
- We evaluated the effect of birth weight on not only BMI, but also fat mass and lean mass.
- Since cross-sectional data was used, inferences about causal effects cannot be made clearly and only
 assumptions about the relationship can be suggested.
- Although parental factors including maternal obesity, diabetes may influence the birth weight of their
 offspring, such information are not included in this survey, and birth weight was self-reported in the
 survey, which may be subject to recall bias.

INTRODUCTION

Obesity in adolescents has been increasing worldwide. The prevalence of obesity among adolescents in Korea increased from 6.8% in 1998 to around 10% in 2005[1,2]. This increase in obesity may be explained by the rapid economic development and westernization of diet in Korea. Meanwhile, obesity in adolescence is not only associated with cardiovascular disease and pulmonary disease, but also has psychosocial consequences[3], with long-lasting effects. Since obesity among adolescents is tightly correlated with later diseases, identifying the risk factors of adolescent obesity and early prevention are imperative. Early life events have been suggested to play an important role in developing obesity by altering the body composition and appetite control by the central nervous system[4]. Also, one's ability to regulate and metabolize nutrients throughout life is known to be determined pre or post-natally, suggesting peri-natal factors may be important predictors of obesity[5].

Among early life factors, birth weight is closely related to intrauterine nutrition[6] and early body composition. Several previous studies have shown that high birth weight increases the risk of obesity in adults[4,7,8] and some added that low birth weight reduces the risk of obesity[4].

However, previous studies about the relationship between birth weight and obesity in adolescents have yielded inconsistent results. Some studies have shown J-shaped or linear associations between birth weight and body mass index (BMI) in childhood[9-11]. On the other hand, other studies have shown no significant relationships between birthweight and BMI[12]. Meanwhile, previous studies on the relationship between birth weight and body composition have shown that birth weight is more-closely related to lean mass compared to fat mass in adolescents in the United Kingdom [13,14], and in Brazilian 9 year-old children[15]. However, despite the differences in body composition according to ethnicity [16,17], few studies have targeted Asian adolescents.

In this study, we investigated the gender-specific associations between birth weight and body composition including BMI, fat mass, and lean mass in adolescents using the data from the fifth Korean National Health and Nutrition Examination Survey of 2010-2011 (KNHANES V).

METHODS

Study population and data collection

KNHANES is a national survey conducted every year by the Ministry of Health and Welfare. KNHANES V was performed from 2010 to 2011, and included 17,476 nationally representative non-institutionalized civilians in Korea. KNHANES V contains data on heath interviews, health behaviors, health examination, nutrition and large-scale whole-body dual energy X-ray absorptiometry (DXA). Target sampling follows a stratified multi-stage clustered probability design. More details on KNHANES have been published previously[18], and the original data are publicly available through the KNHANES website.

Those aged from 12 to 18 years among the participants in the KNHANES V (n=1,510) were initially selected for this study. We excluded participants who did not respond to the birth weight questionnaire (n=203), and those who did not have BMI values (n=3). The final study population included 1,304 individuals (693 men and 611 women) (Figure 1). For the body composition study, only those with DXA examination values (n=884) were used among the study population.

Sociodemographic, biomedical and lifestyle factors

This study considered sociodemographic actors that could affect outcome of the analyses. Age, sex, residential area, and household income were self-reported by the participants. Residential area was categorized into capital, metropolitan area, and town/city. As the study population consisted of adolescents who generally have no income, household income was considered and divided into tertiles.

Assessment of birth weight, body composition and obesity

Birth weight was reported by the participants' mothers in KNHANES V. We categorized participants into three groups according to their percentile of birth weight (0-25%, 25-75%, 75-100%). The cutoff points for each group were 3.00kg, 3.50kg. The middle group in terms of birth weight (25-75%, birth weight between 3.00kg and 3.50kg) was used as the reference.

In KNHANES V, body compositions were measured by skilled technicians, providing accurate and reliable data. All participants changed into light clothing with all jewelry removed, and then underwent DXA examinations. BMI was calculated by dividing weight by height squared (kg/m²). We divided total fat mass and lean mass obtained from DXA examinations by height squared to calculate Fat Mass Index (FMI) and Lean Mass Index (LMI) (kg/m²) for each individual.

We used definition of obesity for Asians proposed by the World Health Organization Western Pacific Region[19]. We classified the study participants into overweight (between 85th and 95th percentiles of BMI of

each age and sex groups or between 23 kg/m²and 25.0 kg/m²) and general obesity (BMI \geq 95th percentile BMI of each age and sex group or greater than 25 kg/m²).

Statistical analysis

All statistical analysis was done using SPSS Statistics 13.0 (IBM Corp., Armonk, NY.) and Stata 13.0 (STATA Corp., College Station, TX, USA). We used multivariable logistic regression in order to calculate the adjusted odds ratio (aOR) and 95% confidence intervals (95% CI) of being overweight and obese according to birth weight. Sociodemographic factors were adjusted. We used the least squares means adjusted for the same co-variates to examine the association between birth weight and body composition for the total study population, men, and women. Based on a multiple linear regression, the linear trend of adjusted means for BMI, FMI and LMI was tested across birth weight. Additionally, we ran a sensitivity analysis imputing the missing data with an expectation-maximization algorithm, as there is a possibility that missing DXA data are nonrandom. By the use of this approach, we could avoid using biased population estimates. Linear trend of adjusted means for BMI, FMI and LMI was tested after imputation.

RESULTS

Characteristics of the study population

General characteristics of the total study population, male participants, and female participants are shown in Table 1. In the total population, the mean birth weight was 3.3kg, and was slightly higher in men than women (3.3kg, 3.2kg, respectively). The prevalence of being overweight and obese was higher in men than in women. The mean values (standard deviation, SD) of FMI in adolescents was $5.8 \ (\pm 2.5) \ \text{kg/m}^2$ in the total population, $5.0 \ (\pm 2.5) \ \text{kg/m}^2$ in men and $6.7 \ (\pm 2.2) \ \text{kg/m}^2$ in women. The mean values (SD) of LMI was $15.0 \ (\pm 2.1) \ \text{kg/m}^2$ in the total population, $16.0 \ (\pm 2.0) \ \text{kg/m}^2$ in men, and $13.8 \ (\pm 1.5) \ \text{kg/m}^2$ in women.

Relationship between birth weight, overweight and obesity

BMI of adolescents tended to increase linearly with increasing birth weight (P for trend: <0.01). Table 2 shows the total and sex-stratified odds ratios of overweight and general obesity according to birth weight. In total population, the unadjusted OR for overweight in the high birth weight group (highest 25th percentile group) was 1.76 (95% CI 1.12-2.79) compared to the reference group. In the adjusted analysis, the high birth weight group also had higher risk of being overweight (aOR 1.64, 95% CI 1.05-2.57) compared to the reference group. In men, the unadjusted OR for overweight was 2.28 (95% CI 1.29-4.04), and the association remained significant after adjustment of co-variates (aOR 2.15, 95% CI 1.21-3.84). However, there was no association between high birth weight and obesity in men (aOR 0.98, 95% CI 0.53-1.82). In contrast, in women, adjusted analysis demonstrated the association between high birth weight and general obesity after adjustment (aOR 2.15, 95% CI 1.06-4.37), but no association with being overweight (aOR 0.91, 95% CI 0.41-2.01).

Relationship between birth weight and body composition

The associations between birth weight, fat mass, and lean mass of total participants, men, and women are presented in Figure 2 Figure 3, and Figure 4, respectively. After adjusting for sociodemographic factors, the least squares means of FMI increased significantly with increasing birth weight in the total population (*P* for trend: 0.03). However, LMI showed no significant increase with increasing birth weight (P for trend: 0.08). In male participants, higher birth weight was neither associated with higher FMI nor LMI (*P* for trend: 0.20, 0.25). In female participants, higher birth weight was associated with higher FMI (*P* for trend: 0.03), while LMI showed an inverse U-shape (*P* for trend: 0.25). We evaluated that even after imputing the missing data, the overall trend of positive correlation between birth weight and FMI did not change. In women and total population, FMI increased significantly with increasing birth weight (P for trend: <0.01 for both). However, LMI did not increase with increasing birth weight (P for trend: 0.20).

Table 1. General characteristics of the study population

	Total (n=1,304)	Men (n=693)	Women (n=611)
Age (year), mean±s.d	14.7 (2.0)	14.7 (2.0)	14.8 (1.9)
Residence			
Capital	284 (21.8)	151 (21.8)	133 (21.8)
Metropolitan	279 (21.4)	148 (21.4)	131 (21.4)
Town/City	741 (56.8)	394 (56.9)	347 (56.8)
Household Income			
Lowest Third	144 (11.2)	64 (9.4)	80 (13.3)
Middle Third	727 (56.6)	385 (56.5)	342 (56.8)
Highest Third	413 (32.2)	233 (34.2)	180 (29.9)
Birth Weight, mean±s.d	3.3 (0.5)	3.3 (0.5)	3.2 (0.5)
Obesity			
Overweight b	162 (12.4)	97 (14.0)	65 (10.6)
General Obesity ^c	171 (13.1)	102 (14.7)	69 (11.3)
Body Composition			
Body Mass Index (kg/m ²), mean±s.d	21.0 (3.7)	21.2 (3.8)	20.7 (3.4)
Fat Mass Index (kg/m ²), mean±s.d	5.8 (2.5)	5.0 (2.5)	6.7 (2.2)
Lean Mass Index (kg/ m ²), mean±s.d	15.0 (2.1)	16.0 (2.0)	13.8 (1.5)

Note: Data presented in number (percentage) with appropriate units unless otherwise stated.

^b Overweight: BMI \geq 85 percentile BMI of age and sex or 23 kg/m², but not obesity

^c General Obesity (Korean criteria): BMI ≥ 95 percentile BMI of age and sex or 25 kg/m²

Table 2: Crude and adjusted analyses of the association between birth weight and obesity in Korean adolescents

	Overweight			General Obesity		
Birth Weight	Proportion n (%)	Crude OR (95% CI)	Adjusted* OR (95% CI)	Proportion n (%)	Crude OR (95% CI)	Adjusted* OR (95% CI)
Men (n=693)						
0-25 % (n=141)	18 (12.8)	1.51 (0.75-3.03)	1.41 (0.68-2.91)	21 (14.9)	1.06 (0.54-2.09)	1.06 (0.54-2.06)
25-75 % (n=354)	44 (12.4)	1 (referent)	1 (referent)	51 (14.4)	1 (referent)	1 (referent)
75-100 % (n=198)	35 (17.7)	2.28 (1.29-4.04)	2.15 (1.21-3.84)	30 (15.2)	0.96 (0.54-1.70)	0.98 (0.53-1.82)
P for trend		0.17	0.17		0.78	0.85
Women (n=611)						
0-25 % (n=163)	15 (9.2)	0.80 (0.38-1.71)	0.81 (0.39-1.68)	17 (10.4)	0.91 (0.44-1.87)	1.00 (0.49-2.07)
25-75 % (n=326)	34 (10.4)	1 (referent)	1 (referent)	33 (10.1)	1 (referent)	1 (referent)
75-100% (n=122)	16 (13.1)	0.91 (0.43-1.91)	0.91 (0.41-2.01)	19 (15.6)	1.92 (0.94-3.91)	2.15 (1.06-4.37)
P for trend		0.72	0.74		0.09	0.09
Total (n=1,304)						
0-25 % (n=304)	33 (10.9)	1.11 (0.67-1.86)	1.13 (0.66-1.91)	38 (12.5)	0.96 (0.59-1.58)	1.04 (0.63-1.70)
25-75 % (n=680)	78 (11.5)	1 (referent)	1 (referent)	84 (12.4)	1 (referent)	1 (referent)
75-100% (n=320)	51 (15.9)	1.76 (1.12-2.79)	1.64 (1.05-2.57)	49 (15.3)	1.27 (0.81-1.99)	1.36 (0.85-2.17)
P for trend		0.11	0.17		0.30	0.33

Acronyms: OR, Odds Ratio; CI, Confidence Intervals

^{*}Adjusted for age, sex, residence, household income.

DISCUSSION

In this cross-sectional study of Korean adolescents, we have shown that birth weight was associated with a higher risk of being overweight in men and obese in women. Also, higher birth weight was associated with greater FMI, but not LMI.

Higher birth weight was associated with increased prevalence of being overweight in the total population and in male adolescents in this study. This result is consistent with the previous cohort studies that showed birth weight is associated with being overweight in male adolescents[12,20]. A recent meta-analysis on birth weight and long-term overweight risk is also consistent with our study that overweight is associated with high birth weight[21].

High birth weight was associated with increased risk of obesity among women, but not in men or the total population. This result differs from previous studies that have shown that high birth weight increased the risk of obesity in adolescents in both men and women[9,11]. However, it was consistent with another study[12] that additionally adjusted family income as our study did. There are also several studies that have shown that higher birth weight is associated with being overweight or obese in children[9,22], and in adults[4,7,8]. It is known that alterations in body fat distribution begins during puberty due to hormones including cortisol, insulin, growth hormone, and sex steroids[23]. The fact that adolescents are physiologically different in body composition from children and adults may account for the differing results from studies that targeted children or adults.

Using the body composition data by DXA, this study found that higher birth weight was related to higher FMI, but not LMI. This contradicts preceding studies which have shown that birth weight is associated with greater lean mass[13-15]. One possible explanation for this trend in increasing fat mass with greater birth weight may be due to the fact that Asians tended to have more fat compared to other ethnicities. It has been shown that BMI and body fat percent is ethnic specific, possibly due to the differences in frame size, relative leg length and physical activity level[16,17,24].

The result of linear relationship between birth weight and later FMI contradicts some of the previous studies that have shown the J- or U-shaped relationships between birth weight and fat mass in later life. Those studies explain their results by the theory that infants who are born small experience rapid catch up growth in early infancy, which results in larger fat mass in later life[25,26]. We could not reveal clear reasons for the difference as we did not have the data of postnatal weight gain, but one possible explanation for this could be ethnic differences as mentioned above. Regarding the possible effects of postnatal weight gain on later body

composition, future studies can be performed to investigate the interaction of birth weight and postnatal weight gain in terms of the effect on later body composition. Through these future studies, whether birth weight or postnatal weight gain velocity are equal or disproportionate contributors to fat mass in later life might be revealed.

One possible explanation for the association between birth weight, obesity, FMI, and LMI is the possibility of common genetic factors. It is said that about 50% of the variance in birth weight and more than 50% of the variance in BMI are attributed to shared genetic factors[27,28]. Therefore, it seems rational to speculate that the genetic factors that made infants heavier could also contribute to the increased risk of greater BMI later in life. Another explanation could be that intrauterine environment, which contributes to birth weight, also affects the formation of the fetal organs involved in energy metabolism by altering the transfer of metabolic substances between mother and fetus[29].

In this study, the relationship between birth weight and both obesity and body composition was different among men and women. Similarly, among previous studies that dealt with relationships between birth weight and possible outcomes in later life including obesity, blood pressure[30], lipid levels[31] and insulin action[32], many have shown gender differences. These findings indicate that men and women could have different mechanisms for body composition. It is suggested that sex steroid hormones alter the body composition during pubertal development[33,34]. Estrogen, for example, is known to play a crucial role in body fat distribution[33]. This difference in hormone actions lead to more increased lean mass in boys, and comparatively high fat mass in girls[35]. Moreover, some studies suggested that bone and muscle growth may be programmed differently by gender during intrauterine life[36,37]. These factors may have contributed to the strong association between birth weight and FMI in women.

High BMI may not be the perfect measure of obesity, as it may not contain accurate information about fat distribution[38]. However, high BMI with high FMI but not LMI, is associated with increased risk of other diseases by reducing the level of immunity. As our study showed that high birth weight is associated with being overweight and obese, with higher FMI compared to LMI, those born with high birth weight should be closely monitored for obesity. If infants are born with high birth weight, early intervention may be needed against obesity through diet and physical activity level at a young age.

There are several limitations in this study. First, since cross-sectional data was used, inferences about causal effects cannot be made clearly and only assumptions about the relationship can be suggested. Although the fact that the outcome, obesity and body composition, could not possibly have occurred prior to the exposure,

birth weight, helps us infer the direction of causality, further studies are needed to clarify the causality and its mechanism. Secondly, birth weight was self-reported in a survey, which means that the data could be less accurate compared to birth records. Although parental factors including maternal obesity, diabetes may influence the birth weight of their offspring, such information are not included in this survey. Despite these limitations, we used a large study population (n=1,304) compared to previous studies, which increases credibility of this study. We also tried to account for missing parental factors by adjusting for household income. Moreover, to the best of our knowledge, there were no preceding studies that adjusted for as many related variables as we did, which increases credibility of this study. Most importantly, this study targeted Koreans, an ethnicity few previous studies have investigated upon, suggesting that ethnic differences and gender differences may exist in the body composition and in the risk of developing obesity.

CONCLUSION

The results of our study suggest that high birth weight may be an indicator of being overweight in Korean adolescents. Particularly in women, high birth weight is associated with general obesity. High birth weight was associated with greater fat mass compared to lean mass. These findings suggest that those born with high birth weight, may be more susceptible to being overweight and obese and may merit close monitoring and early intervention against obesity.



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CONTRIBUTORSHIP

In this study, Myunggee Kang designed the study, analyzed the data, interpreted the results and wrote the paper as a first author. Jung Eun Yoo and Seulggie Choi contributed to data analysis and result interpretation. Kyuwoong Kim contributed to data analysis and literature research. Sang Min Park contributed to study design and results interpretation. All authors were involved in revising the paper and approved the final paper as submitted.

CONFLICT OF INTEREST STATEMENT

No conflict of interest was declared.

ETHICAL APPROVAL

This study did not need ethical approval of our Institutional Review Board, since the survey data examined were publicly available.

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DATA SHARING

All relevant materials are provided in the manuscript. KNHANES V, raw data used in this is available from http://knhanes.cdc.go.kr.

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- Figure 1: Flow Diagram of the Selection Procedure for the Study Population
- **Figure 2:** Least-squares means of FMI and LMI in total participants (n=884). We adjusted for age, sex, residence and household income according to birth weight.
- **Figure 3:** Least-squares means of FMI and LMI in male participants (n=407). We adjusted for age, sex, residence and household income according to birth weight.
- **Figure 4:** Least-squares means of FMI and LMI in female participants (n=477). We adjusted for age, sex, residence and household income according to birth weight.



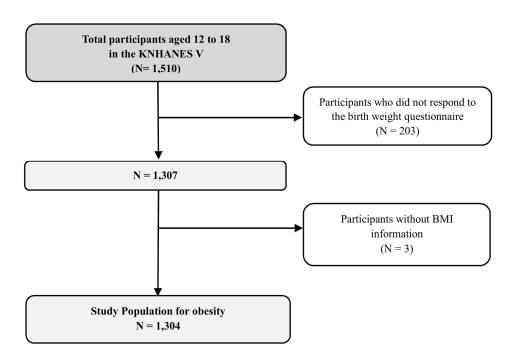


Figure 1: Flow Diagram of the Selection Procedure for the Study Population $87x59mm (600 \times 600 DPI)$

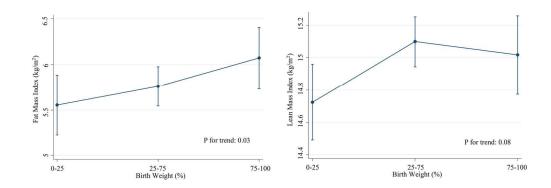


Figure 2: Least-squares means of FMI and LMI in total participants (n=884). We adjusted for sex, age, residence and household income.

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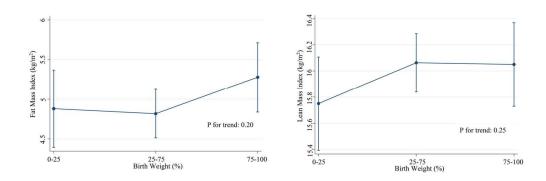


Figure 3: Least-squares means of FMI and LMI in female participants (n=407). We adjusted for sex, age, residence and household income.

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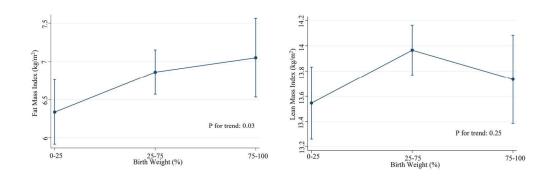


Figure 4: Least-squares means of FMI and LMI in male participants (n=477). We adjusted for sex, age, residence and household income.



STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	Data removed
		(d) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	5
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8
		(b) Indicate number of participants with missing data for each variable of interest	5
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(b) Report category boundaries when continuous variables were categorized	5,6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11,12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10,11
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Associations Between Birth Weight, Obesity, Fat Mass and Lean Mass in Korean Adolescents: The Fifth Korea National Health and Nutrition Examination Survey

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SCHOLARONE™ Manuscripts Associations Between Birth Weight, Obesity, Fat Mass and Lean Mass in Korean Adolescents: The Fifth Korea National Health and Nutrition Examination Survey

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ABSTRACT

Objective

Previous studies on the relationship between birth weight and obesity in adolescents have mostly been conducted within Western populations and have yielded inconsistent results. We aimed to investigate the association between birth weight, obesity, fat mass and lean mass in Korean adolescents using the fifth Korea National Health and Nutritional Examination Survey (KNHANES V).

Methods

The study population consisted of a total of 1,304 (693 men and 611 women) participants aged between 12 and 18 years. Adjusted odds ratio (aORs) and 95% confidence intervals (CIs) were calculated by multivariable logistic regression analyses to determine the association between birth weight and being overweight or obese. Furthermore, adjusted mean values for body mass index (BMI), fat mass index (FMI), and lean mass index (LMI) according to birth weight were calculated by multiple linear regression analyses.

Results

Individuals within the highest 25th percentile in birth weight were more likely to be overweight (aOR=1.64, 95% CI=1.05-2.57) compared to adolescents within the 25th and 75th percentile in birth weight. Female adolescents who were in the highest 25th percentile in birth weight were more likely to be obese (aOR=2.15, 95% CI=1.06-4.37) compared to those within the 25th and 75th percentile in birth weight. Increasing FMI, but not LMI was associated with increasing birth weight (P for trend: 0.03). This tendency remained only in female population in sex stratified analysis (P for trend: 0.03).

Conclusions

High birth weight may lead to obesity and increased fat mass, but not lean mass. Adolescents born with high birth weight may benefit from close weight monitoring and early intervention against obesity.

Keywords: birth weight, obesity, body composition, fat mass, lean mass

Strengths and limitations of this study

- The study population of this study consisted of Koreans, an ethnicity few previous studies targeted,
 and was relatively large (1,304 participants), raising the credibility of this study.
- We evaluated the effect of birth weight on not only BMI, but also fat mass and lean mass.
- Since observational data was used, inferences about causal effects cannot be made clearly and only
 assumptions about the relationship can be suggested.
- Parental factors such as maternal obesity and diabetes that may influence the birth weight of the
 offspring were not included in the survey. Furthermore, birth weight, which was self-reported in the
 survey, may be subject to recall bias.

INTRODUCTION

Obesity among children and adolescents have increased in prevalence from around 16.5% in 1980 to around 23.0% in 2013 in developed countries[1]. This dramatic increase in obesity is also shown in Korea, with an increase in prevalence of 6.8% in 1998 to around 10.0% in 2005[2,3]. Obesity in adolescence is not only associated with cardiovascular disease and pulmonary disease, but also has psychosocial consequences[4] that may have long-lasting implications well into adulthood. Therefore, identifying and controlling risk factors of adolescent obesity is imperative in reducing the risk of serious illnesses later in life. Meanwhile, early life events have been suggested to play an important role in developing obesity by altering the body composition and control in appetite[5]. Furthermore, as one's ability to regulate and metabolize nutrients is determined pre or post-natally, peri-natal factors may be important predictors of obesity[6].

Among peri-natal factors, birth weight is closely related to intrauterine nutrition[7] and early body composition. Several previous studies investigating the relationship between birth weight and obesity in adolescents have yielded inconsistent results. While some studies have shown J-shaped or linear associations between birth weight and body mass index (BMI) in childhood[8-10], other studies have shown no significant relationships between birthweight and BMI[11]. In terms of the association between birth weight and body composition, previous studies have shown that birth weight is more-closely related to lean mass compared to fat mass in adolescents in the United Kingdom[12,13], and in Brazilian 9 year-old children[14]. Interestingly, relatively few studies have investigated the association between birth weight and body composition in an Asian population. As there are innate differences in body composition according to ethnicity[15,16], studies determining the association between birth weight and body compositions are needed.

Therefore, we investigated the association between birth weight, obesity and body composition including fat mass, and lean mass in adolescents using the fifth Korean National Health and Nutrition Examination Survey of 2010-2011 (KNHANES V).

METHODS

Study population and data collection

KNHANES is a national survey conducted every year by the Ministry of Health and Welfare. KNHANES V was performed from 2010 to 2011, and included 17,476 nationally representative non-institutionalized civilians in Korea. KNHANES V contains data on heath interviews, health behaviours, health examination, nutrition and large-scale whole-body dual energy X-ray absorptiometry (DXA). Target sampling follows a stratified multi-stage clustered probability design. Details on KNHANES can be found elsewhere[17], and the original data are publicly available via the KNHANES website.

Participants aged from 12 to 18 years (n=1,510) were initially selected for this study. We excluded participants who did not respond to the birth weight questionnaire (n=203), and those who did not have BMI values (n=3). The final study population included 1,304 individuals (693 men and 611 women) (Figure 1). For the body composition study, only those with DXA examination values (n=884) were used.

Sociodemographic factors

This study considered sociodemographic factors that could affect the outcome of the analyses. Age, sex, residential area, and household income, all of which were self-reported, were included in the analyses. Residential area was categorized into capital, metropolitan area, and town/city. Household income was divided into tertiles.

Assessment of birth weight, body composition and obesity

Birth weight was reported by the participants' mothers. We categorized participants into three groups according to their percentile of birth weight (0-25%, 25-75%, 75-100%). The cutoff points for each group were 3.00 kg and 3.50 kg. The middle group in terms of birth weight (25-75%, birth weight between 3.00kg and 3.50kg) was used as the reference group.

BMI was calculated by dividing weight by height squared (kg/m²). Body composition was measured by DXA examinations, which were conducted by skilled technicians. We divided total fat mass and lean mass obtained from DXA examinations by height squared to calculate fat mass index (FMI) and lean mass index (LMI) (kg/m²) for each individual.

We defined obesity according to the guidelines by the World Health Organization Western Pacific Region[18]. We classified the study participants into being overweight (between 85^{th} and 95^{th} percentiles of BMI of each age and sex groups or between 23 kg/m^2 and 25 kg/m^2) and being obese (BMI $\geq 95^{th}$ percentile BMI of each age and sex group or greater than 25 kg/m^2).

Statistical analysis

All statistical analyses were conducted using SPSS Statistics 23 (IBM Corp., Armonk, NY.) and Stata 13.0 (STATA Corp., College Station, TX, USA). The association between birth weight, being overweight, and being obese was determined by adjusted odds ratio (aORs) and 95% confidence intervals (CIs) calculated by logistic regression analysis. Factors such as sex, age, residence and household income were adjusted for. The association between birth weight and the adjusted mean values of BMI and body composition was determined by linear regression analysis. Additionally, we ran a sensitivity analysis imputing the missing data as there is a possibility that missing data are non-random. Five imputations for missing data were performed with the use of the Markov chain Monte Carlo multiple imputation technique. Variables adjusted for the primary analysis were included for imputation. The pooled effect on the primary outcome was analysed after multiple imputation. A P value of less than 0.05 was considered statistically significant.

RESULTS

Characteristics of the study population

The general characteristics of the total study population, male participants, and female participants are shown in Table 1. In the total population, the mean birth weight was 3.3 kg, and was slightly higher in men compared to women (3.3 kg, 3.2 kg respectively). The prevalence of being overweight and obese was higher in men than in women (overweight: 14.0%, 10.6% respectively; obesity: 14.7%, 11.3% respectively). The mean values (standard deviation, SD) of FMI in adolescents was $5.8 \ (\pm 2.5) \ kg/m^2$ in the total population, $5.0 \ (\pm 2.5) \ kg/m^2$ in men and $6.7 \ (\pm 2.2) \ kg/m^2$ in women. The mean values (SD) of LMI was $15.0 \ (\pm 2.1) \ kg/m^2$ in the total population, $16.0 \ (\pm 2.0) \ kg/m^2$ in men, and $13.8 \ (\pm 1.5) \ kg/m^2$ in women.

Table 2 describes characteristics of three groups: those with complete data (n=884), those with missing values on birth weight or BMI (n=206), and those with missing values on DXA (n=420). There were no significant differences in the distribution of characteristics, including birth weight, BMI, FMI and LMI among the three groups. However, those without birth weight data had higher percentage of those living in the capital area, and being in the lowest tertile of household income compared to those with complete data. Furthermore, both of the distribution of area of residence and household income differed significantly from the complete case (P value <0.01 for both area of residence and household income).

Relationship between birth weight, BMI, overweight and obesity

BMI of adolescents tended to increase linearly with increasing birth weight in total participants, men and women (P for trend: <0.01, 0.02, and 0.05 respectively) as presented in Figure 2. Table 3 shows the total and sex-stratified ORs of being overweight and being obese according to birth weight. In the total population, the unadjusted OR for overweight in the high birth weight group (highest 25th percentile group) was 1.76 (95% CI 1.12-2.79) compared to the reference group. In the adjusted analysis, the high birth weight group also had higher risk of being overweight (aOR 1.64, 95% CI 1.05-2.57) compared to the reference group. In men, the unadjusted OR for being overweight was 2.28 (95% CI 1.29-4.04), and the association remained significant after adjustment of co-variates (aOR 2.15, 95% CI 1.21-3.84). However, there was no association between high birth weight and obesity in men (aOR 0.98, 95% CI 0.53-1.82). In contrast, in women, adjusted analysis demonstrated the association between high birth weight and being obese after adjustment (aOR 2.15, 95% CI 1.06-4.37), but no association with being overweight (aOR 0.91, 95% CI 0.41-2.01). After data imputation, results that were significant in the complete case analysis remained consistent. In the total population and male population, the high birth weight group had higher risk of being overweight (aOR 1.43, 95% CI 1.11-2.03; aOR

2.04, 95% CI 1.15-2.89) compared to the reference group after adjustment. In female population, high birth weight group had higher risk of being obese (aOR 1.84, 95% CI 1.26-2.67) compared to the reference group after adjustment.

Relationship between birth weight and body composition

The associations between birth weight, fat mass, and lean mass are presented in Figure 3 (total participants), Figure 4 (men), and Figure 5 (women). After adjusting for sociodemographic factors, the adjusted mean values of FMI increased significantly with increasing birth weight in the total population (P for trend: 0.03). However, LMI showed no significant increase with increasing birth weight (P for trend: 0.08). In male participants, higher birth weight was neither associated with higher FMI nor LMI (P for trend: 0.20, 0.25 respectively). In female participants, higher birth weight was associated with higher FMI (P for trend: 0.03), while LMI showed an inverse U-shape (P for trend: 0.25). Even after imputing the missing data, the overall trend of positive correlation between birth weight and FMI did not change. In women and the total population, FMI increased significantly with increasing birth weight (P for trend: <0.01 for both women and the total population). However, LMI did not increase with increasing birth weight (P for trend: 0.20).

Table 1. General characteristics of the study population

	Total (n=1,304)	Men (n=693)	Women (n=611)	
Age (year), mean±s.d	14.7 (2.0)	14.7 (2.0)	14.8 (1.9)	
Residence				
Capital	284 (21.8)	151 (21.8)	133 (21.8)	
Metropolitan	279 (21.4)	148 (21.4)	131 (21.4)	
Town/City	741 (56.8)	394 (56.9)	347 (56.8)	
Household Income				
Lowest Third	144 (11.2)	64 (9.4)	80 (13.3)	
Middle Third	727 (56.6)	385 (56.5)	342 (56.8)	
Highest Third	413 (32.2)	233 (34.2)	180 (29.9)	
Birth Weight, mean±s.d	3.3 (0.5)	3.3 (0.5)	3.2 (0.5)	
Obesity				
Overweight ^a	162 (12.4)	97 (14.0)	65 (10.6)	
General Obesity b	171 (13.1)	102 (14.7)	69 (11.3)	
Body Composition				
Body Mass Index (kg/m ²), mean±s.d	21.0 (3.7)	21.2 (3.8)	20.7 (3.4)	
Fat Mass Index (kg/m ²), mean±s.d	5.8 (2.5)	5.0 (2.5)	6.7 (2.2)	
Lean Mass Index (kg/ m ²), mean±s.d	15.0 (2.1)	16.0 (2.0)	13.8 (1.5)	

Note: Data presented in number (percentage) with appropriate units unless otherwise stated.

^a Overweight: BMI ≥ 85 percentile BMI of age and sex or 23 kg/m², but not obesity

Table 2. Comparison of general characteristics between complete cases and cases with missing data

	Complete Case (n=884)	Missing Case ^c (n=206)	P value d	Missing Case ^e (n=420)	P value f
Age (year), mean±s.d	14.7 (1.9)	14.9 (2.0)	0.13	14.8 (2.0)	0.19
Residence			< 0.01		0.28
Capital	191 (21.6)	68 (33.0)		93 (22.1)	
Metropolitan	179 (20.3)	42 (20.4)		100 (23.8)	
Town/City	514 (58.1)	96 (46.6)		227 (54.1)	
Household Income			< 0.01		0.56
Lowest Third	103 (11.9)	54 (27.1)		41 (9.9)	
Middle Third	487 (56.1)	99 (49.8)		240 (57.7)	
Highest Third	278 (32.0)	46 (23.1)		135 (32.5)	
Birth Weight, mean±s.d	3.2 (0.5)	3.0 (0.8)	0.33	3.3 (0.5)	0.07
Obesity					
Overweight ^a	117 (13.2)	9 (10.3)	0.57	45 (10.7)	0.20
General Obesity b	114 (12.9)	10 (11.5)	0.66	57 (13.6)	0.74
Body Composition					
Body Mass Index (kg/m ²), mean±s.d	20.9 (3.6)	20.4 (3.5)	0.13	21.0 (3.7)	0.72
Fat Mass Index (kg/m ²), mean±s.d	5.8 (2.5)	5.3 (2.5)	0.15	. ,	
Lean Mass Index (kg/ m ²), mean±s.d	15.0 (2.1)	15.2 (2.3)	0.36		

Note: Data presented in number (percentage) with appropriate units unless otherwise stated.

^a Overweight: BMI ≥ 85 percentile BMI of age and sex or 23 kg/m², but not obesity

^b General Obesity (Korean criteria): BMI ≥ 95 percentile BMI of age and sex or 25 kg/m²

^c Cases with missing values on birth weight or bmi (cases removed from obesity analysis)

^d P value of the difference between complete case and missing case ^c

^e Cases with missing values on DXA (cases removed from body composition analysis)

^fP value of the difference between complete case and missing case ^e

Table 3: Crude and adjusted analyses of the association between birth weight and obesity in Korean adolescents

	Overweight				General Obesity			
Birth Weight	Crude Prevalence n (%)	Weighted ^a Prevalence %	Crude OR (95% CI)	Adjusted ^b OR (95% CI)	Crude Prevalence n (%)	Weighted ^a Prevalence %	Crude OR (95% CI)	Adjusted ^b OR (95% CI)
Men (n=693)								
0-25 % (n=141)	18 (12.8)	14.9	1.51 (0.75-3.03)	1.41 (0.68-2.91)	21 (14.9)	15.0	1.06 (0.54-2.09)	1.06 (0.54-2.06)
25-75 % (n=354)	44 (12.4)	10.4	1 (referent)	1 (referent)	51 (14.4)	14.3	1 (referent)	1 (referent)
75-100 % (n=198)	35 (17.7)	21.0	2.28 (1.29-4.04)	2.15 (1.21-3.84)	30 (15.2)	13.7	0.96 (0.54-1.70)	0.98 (0.53-1.82)
P for trend			0.17	0.17			0.78	0.85
Women (n=611)								
0-25 % (n=163)	15 (9.2)	8.2	0.80 (0.38-1.71)	0.81 (0.39-1.68)	17 (10.4)	10.0	0.91 (0.44-1.87)	1.00 (0.49-2.07)
25-75 % (n=326)	34 (10.4)	10.1	1 (referent)	1 (referent)	33 (10.1)	10.9	1 (referent)	1 (referent)
75-100% (n=122)	16 (13.1)	9.2	0.91 (0.43-1.91)	0.91 (0.41-2.01)	19 (15.6)	19.1	1.92 (0.94-3.91)	2.15 (1.06-4.37)
P for trend			0.72	0.74			0.09	0.09
Total (n=1,304)								
0-25 % (n=304)	33 (10.9)	11.3	1.11 (0.67-1.86)	1.13 (0.66-1.91)	38 (12.5)	12.3	0.96 (0.59-1.58)	1.04 (0.63-1.70)
25-75 % (n=680)	78 (11.5)	10.3	1 (referent)	1 (referent)	84 (12.4)	12.7	1 (referent)	1 (referent)
75-100% (n=320)	51 (15.9)	16.8	1.76 (1.12-2.79)	1.64 (1.05-2.57)	49 (15.3)	15.6	1.27 (0.81-1.99)	1.36 (0.85-2.17)
P for trend			0.11	0.17			0.30	0.33

Acronyms: OR, Odds Ratio; CI, Confidence Intervals

^a Prevalence after applying sampling weights

^b Adjusted for age, sex, residence, household income.

DISCUSSION

In this cross-sectional study of Korean adolescents, we have shown that higher birth weight was associated with a higher risk of being overweight in men and obese in women. Also, higher birth weight was associated with greater BMI and FMI, but not LMI.

Higher birth weight was associated with increased risk of being overweight in the total population and in male adolescents. This is consistent with previous cohort studies that showed birth weight is associated with being overweight in male adolescents[11,19]. A recent meta-analysis on birth weight and long-term overweight risk is also consistent with our study that overweight is associated with high birth weight[20]. Furthermore, high birth weight was associated with increased risk of obesity among women, but not in men or the total population. This differs from previous studies that have shown that high birth weight increased the risk of obesity in adolescents in both men and women[8,10]. However, it was consistent with another study[11] that additionally adjusted for family income. Several other studies have shown that higher birth weight is associated with being overweight or obese in children[8,21], and in adults[5,22,23]. It is known that alterations in body fat distribution begin during puberty due to hormones including cortisol, insulin, growth hormone, and sex steroids[24]. The fact that adolescents are physiologically different in body composition from children and adults may account for the differing results from studies that targeted children or adults.

Higher birth weight was related to higher FMI, but not LMI. This contradicts preceding studies which have shown that higher birth weight is associated with greater lean mass[12-14]. One possible explanation for this trend in increasing fat mass but not lean mass with greater birth weight may be due to the fact that Asians tended to have greater proportions of fat compared to other ethnicities. It has been shown that BMI and body fat percent are ethnic specific, possibly due to the differences in frame size, relative leg length and physical activity level[15,16,25].

The linear relationship between birth weight and FMI contradicts some of the previous studies that have shown J- or U-shaped relationships between birth weight and fat mass[8,26,27]. Previous studies have attempted to explain the J- or U-shaped relationship between birth weight and fat mass by citing studies that show infants who are born small experience rapid catch up growth in early infancy, which results in larger fat mass in later life[28,29]. While we could not reveal clear reasons for the discrepancy in our results compared to previous studies as we did not have information on postnatal weight gain, one possible explanation may be due to the ethnic differences of body composition as mentioned previously. Future studies investigating the

association between birth weight and postnatal weight gain in terms of the effect of body composition are needed.

The significant association between birth weight, obesity, FMI, and LMI may be explained by genetic factors. It is said that about 50% of the variance in birth weight and more than 50% of the variance in BMI are attributed to shared genetic factors[30,31]. Therefore, it seems rational to speculate that the genetic factors that made infants heavier could also contribute to the increased risk of greater BMI later in life. Another explanation could be that intrauterine environment, which contributes to birth weight, also affects the formation of the fetal organs involved in energy metabolism by altering the transfer of metabolic substances between mother and fetus[32].

In this study, the relationship between birth weight and both obesity and body composition was different among men and women. Similarly, among previous studies that dealt with relationships between birth weight and possible outcomes in later life including obesity, blood pressure[33], lipid levels[34] and insulin action[35], many have shown gender differences. As those factors, such as metabolic variables and blood pressure, are closely related to body composition[36-38], these findings indicate that men and women could have different mechanisms for body composition. It is suggested that sex steroid hormones alter the body composition during pubertal development[39,40]. Estrogen, for example, is known to play a crucial role in body fat distribution[39]. This difference in hormone actions lead to more increased lean mass in boys, and comparatively high fat mass in girls[41]. Moreover, some studies suggested that bone and muscle growth may be programmed differently by gender during intrauterine life[42,43]. These factors may have contributed to the strong association between birth weight and FMI in women.

There are several limitations in this study. First, since observational data was used, inferences about causal effects cannot be made clearly and only assumptions about the relationship can be suggested. Further studies are needed to clarify the causality and its mechanism. Secondly, birth weight was self-reported in a survey, which means that the data could be less accurate compared to birth records. Although parental factors including maternal obesity, diabetes may influence the birth weight of their offspring, such information are not included in this survey. Despite these limitations, we tried to account for parental factors by adjusting for household income. Also, we used a large study population (n=1,304) and performed sensitivity analysis, which makes our study generalisable to the Korean population, while further studies on other population are recommended to apply the results to other ethnics. Most importantly, this study targeted Koreans, an ethnicity

few previous studies have investigated upon, suggesting that ethnic differences and gender differences may exist in the body composition and in the risk of developing obesity.



CONCLUSION

The results of our study suggest that high birth weight may be an indicator of being overweight in Korean adolescents. Particularly in women, high birth weight is associated with higher risk of general obesity. High birth weight was associated with greater fat mass compared to lean mass. These findings suggest that those born with high birth weight, may be more susceptible to being overweight and obese and may merit close monitoring and early intervention against obesity.



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CONTRIBUTORSHIP

In this study, Myunggee Kang designed the study, analysed the data, interpreted the results and wrote the paper as a first author. Jung Eun Yoo and Seulggie Choi contributed to data analysis and result interpretation. Kyuwoong Kim contributed to data analysis and literature research. Sang Min Park contributed to study design and results interpretation. All authors were involved in revising the paper and approved the final paper as submitted.

CONFLICT OF INTEREST STATEMENT

No conflict of interest was declared.

ETHICAL APPROVAL

This study did not need ethical approval of our Institutional Review Board, since the survey data examined were publicly available.

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DATA SHARING

All relevant materials are provided in the manuscript. KNHANES V, raw data used in this is available from http://knhanes.cdc.go.kr.

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- Figure 1: Flow Diagram of the Selection Procedure for the Study Population
- **Figure 2:** Least-squares means of BMI in total participants (n=1304), male (n=693), and female (n=611). We adjusted for age, sex, residence and household income according to birth weight.
- **Figure 3:** Least-squares means of FMI and LMI in total participants (n=884). We adjusted for age, sex, residence and household income according to birth weight.
- **Figure 4:** Least-squares means of FMI and LMI in male participants (n=407). We adjusted for age, sex, residence and household income according to birth weight.
- **Figure 5:** Least-squares means of FMI and LMI in female participants (n=477). We adjusted for age, sex, residence and household income according to birth weight.

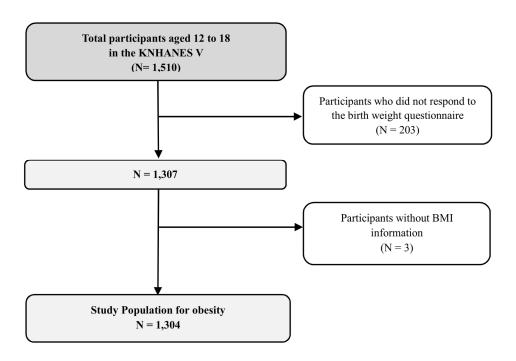


Figure 1: Flow Diagram of the Selection Procedure for the Study Population $87x59mm (600 \times 600 DPI)$

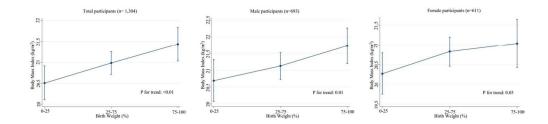


Figure 2: Least-squares means of BMI in total participants (n=1304), male (n=693), and female (n=611). We adjusted for age, sex, residence and household income according to birth weight.

57x13mm (600 x 600 DPI)

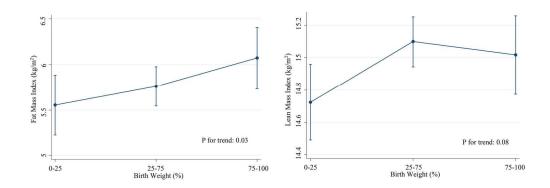


Figure 3: Least-squares means of FMI and LMI in total participants (n=884). We adjusted for age, sex, residence and household income according to birth weight.



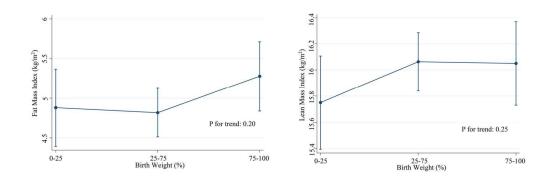


Figure 4: Least-squares means of FMI and LMI in male participants (n=407). We adjusted for age, sex, residence and household income according to birth weight.



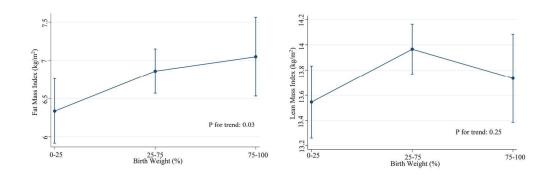


Figure 5: Least-squares means of FMI and LMI in female participants (n=477). We adjusted for age, sex, residence and household income according to birth weight.



STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	5,6
		(d) If applicable, describe analytical methods taking account of sampling strategy	6
		(e) Describe any sensitivity analyses	6
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	5
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers of outcome events or summary measures	7,8,9
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(b) Report category boundaries when continuous variables were categorized	5,6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7,8
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12,13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Associations Between Birth Weight, Obesity, Fat Mass and Lean Mass in Korean Adolescents: The Fifth Korea National Health and Nutrition Examination Survey

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SCHOLARONE™ Manuscripts Associations Between Birth Weight, Obesity, Fat Mass and Lean Mass in Korean Adolescents: The Fifth Korea National Health and Nutrition Examination Survey

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ABSTRACT

Objective

Previous studies on the relationship between birth weight and obesity in adolescents have mostly been conducted within Western populations and have yielded inconsistent results. We aimed to investigate the association between birth weight, obesity, fat mass and lean mass in Korean adolescents using the fifth Korea National Health and Nutritional Examination Survey (KNHANES V).

Methods

The study population consisted of a total of 1,304 (693 men and 611 women) participants aged between 12 and 18 years. Adjusted odds ratio (aORs) and 95% confidence intervals (CIs) were calculated by multivariable logistic regression analyses to determine the association between birth weight and being overweight or obese. Furthermore, adjusted mean values for body mass index (BMI), fat mass index (FMI), and lean mass index (LMI) according to birth weight were calculated by multiple linear regression analyses.

Results

Individuals within the highest 25th percentile in birth weight were more likely to be overweight (aOR=1.75, 95% CI=1.11-2.76) compared to adolescents within the 25th and 75th percentile in birth weight. Female adolescents who were in the highest 25th percentile in birth weight were more likely to be obese (aOR=2.13, 95% CI=1.03-4.41) compared to those within the 25th and 75th percentile in birth weight. Increasing FMI, but not LMI was associated with increasing birth weight (P for trend: 0.03). This tendency remained only in female population in sex stratified analysis (P for trend: 0.03).

Conclusions

High birth weight may lead to obesity and increased fat mass, but not lean mass. Adolescents born with high birth weight may benefit from close weight monitoring and early intervention against obesity.

Keywords: birth weight, obesity, body composition, fat mass, lean mass

Strengths and limitations of this study

- The study population of this study consisted of Koreans, an ethnicity few previous studies targeted,
 and was relatively large (1,304 participants), raising the credibility of this study.
- We evaluated the effect of birth weight on not only BMI, but also fat mass and lean mass.
- Since observational data was used, inferences about causal effects cannot be made clearly and only
 assumptions about the relationship can be suggested.
- Parental factors such as maternal obesity and diabetes that may influence the birth weight of the
 offspring were not included in the survey. Furthermore, birth weight, which was self-reported in the
 survey, may be subject to recall bias.

INTRODUCTION

Obesity among children and adolescents have increased in prevalence from around 16.5% in 1980 to around 23.0% in 2013 in developed countries[1]. This dramatic increase in obesity is also shown in Korea, with an increase in prevalence of 6.8% in 1998 to around 10.0% in 2005[2,3]. Obesity in adolescence is not only associated with cardiovascular disease and pulmonary disease, but also has psychosocial consequences[4] that may have long-lasting implications well into adulthood. Therefore, identifying and controlling risk factors of adolescent obesity is imperative in reducing the risk of serious illnesses later in life. Meanwhile, early life events have been suggested to play an important role in developing obesity by altering the body composition and control in appetite[5]. Furthermore, as one's ability to regulate and metabolize nutrients is determined pre or post-natally, peri-natal factors may be important predictors of obesity[6].

Among peri-natal factors, birth weight is closely related to intrauterine nutrition[7] and early body composition. Several previous studies investigating the relationship between birth weight and obesity in adolescents have yielded inconsistent results. While some studies have shown J-shaped or linear associations between birth weight and body mass index (BMI) in childhood[8-10], other studies have shown no significant relationships between birthweight and BMI[11]. In terms of the association between birth weight and body composition, previous studies have shown that birth weight is more-closely related to lean mass compared to fat mass in adolescents in the United Kingdom[12,13], and in Brazilian 9 year-old children[14]. Interestingly, relatively few studies have investigated the association between birth weight and body composition in an Asian population. As there are innate differences in body composition according to ethnicity[15,16], studies determining the association between birth weight and body compositions are needed.

Therefore, we investigated the association between birth weight, obesity and body composition including fat mass, and lean mass in adolescents using the fifth Korean National Health and Nutrition Examination Survey of 2010-2011 (KNHANES V).

METHODS

Study population and data collection

KNHANES is a national survey conducted every year by the Ministry of Health and Welfare. KNHANES V was performed from 2010 to 2011, and included 17,476 nationally representative non-institutionalized civilians in Korea. KNHANES V contains data on heath interviews, health behaviours, health examination, nutrition and large-scale whole-body dual energy X-ray absorptiometry (DXA). Target sampling follows a stratified multi-stage clustered probability design. Details on KNHANES can be found elsewhere[17], and the original data are publicly available via the KNHANES website.

Participants aged from 12 to 18 years (n=1,510) were initially selected for this study. We excluded participants who did not respond to the birth weight questionnaire (n=203), and those who did not have BMI values (n=3). The final study population included 1,304 individuals (693 men and 611 women) (Figure 1). For the body composition study, only those with DXA examination values (n=884) were used.

Sociodemographic factors

This study considered sociodemographic factors that could affect the outcome of the analyses. Age, sex, residential area, and household income, all of which were self-reported, were included in the analyses. Residential area was categorized into capital, metropolitan area, and town/city. Household income was divided into tertiles.

Assessment of birth weight, body composition and obesity

Birth weight was reported by the participants' mothers. We categorized participants into three groups according to their percentile of birth weight (0-25%, 25-75%, 75-100%). The cutoff points for each group were 3.00 kg and 3.50 kg. The middle group in terms of birth weight (25-75%, birth weight between 3.00kg and 3.50kg) was used as the reference group.

BMI was calculated by dividing weight by height squared (kg/m²). Body composition was measured by DXA examinations, which were conducted by skilled technicians. We divided total fat mass and lean mass obtained from DXA examinations by height squared to calculate fat mass index (FMI) and lean mass index (LMI) (kg/m²) for each individual.

We defined obesity according to the guidelines by the World Health Organization Western Pacific Region[18]. We classified the study participants into being overweight (between 85^{th} and 95^{th} percentiles of BMI of each age and sex groups or between 23 kg/m^2 and 25 kg/m^2) and being obese (BMI $\geq 95^{th}$ percentile BMI of each age and sex group or greater than 25 kg/m^2).

Statistical analysis

All statistical analyses were conducted using SPSS Statistics 23 (IBM Corp., Armonk, NY.) and Stata 13.0 (STATA Corp., College Station, TX, USA). The association between birth weight, being overweight, and being obese was determined by adjusted odds ratio (aORs) and 95% confidence intervals (CIs) calculated by logistic regression analysis. Participants being neither overweight nor obese were used as a "noncase" in both overweight and obesity analyses. Factors such as sex, age, residence and household income were adjusted for. The association between birth weight and the adjusted mean values of BMI and body composition was determined by linear regression analysis.

Additionally, we ran a sensitivity analysis imputing the missing data as there is a possibility that missing data are non-random. Markov chain Monte Carlo multiple imputation technique was used to create forty datasets, following conservative recommendations[19]. In addition to variables included in the primary analyses (e.g. sociodemographic factors, birthweight, BMI, and DXA data), health behaviours information (e.g. smoking, drinking, physical activity, and energy consumption) and health status related to obesity (e.g. hypertension, diabetes, asthma, and impaired fasting glucose) were included as auxiliary variables. The pooled effect on the primary outcome was analysed after multiple imputation. For all analyses, a P value of less than 0.05 was considered statistically significant.

RESULTS

Characteristics of the study population

The general characteristics of the total study population, male participants, and female participants are shown in Table 1. In the total population, the mean birth weight was 3.3 kg, and was slightly higher in men compared to women (3.3 kg, 3.2 kg respectively). The prevalence of being overweight and obese was higher in men than in women (overweight: 14.0%, 10.6% respectively; obesity: 14.7%, 11.3% respectively). The mean values (standard deviation, SD) of FMI in adolescents was $5.8 \ (\pm 2.5) \ kg/m^2$ in the total population, $5.0 \ (\pm 2.5) \ kg/m^2$ in men and $6.7 \ (\pm 2.2) \ kg/m^2$ in women. The mean values (SD) of LMI was $15.0 \ (\pm 2.1) \ kg/m^2$ in the total population, $16.0 \ (\pm 2.0) \ kg/m^2$ in men, and $13.8 \ (\pm 1.5) \ kg/m^2$ in women.

Table 2 describes characteristics of three groups: those with complete data (n=884), those with missing values on birth weight or BMI (n=206), and those with missing values on DXA (n=420). There were no significant differences in the distribution of characteristics, including birth weight, BMI, FMI and LMI among the three groups. However, those without birth weight or BMI data had higher percentage of those living in the capital area, and being in the lowest tertile of household income compared to those with complete data. Furthermore, both of the distribution of area of residence and household income differed significantly from the complete case (P value <0.01 for both area of residence and household income).

Relationship between birth weight, BMI, overweight and obesity

BMI of adolescents tended to increase linearly with increasing birth weight in total participants, men and women (P for trend: <0.01, 0.01, and 0.05 respectively) as presented in Figure 2. Table 3 shows the total and sex-stratified ORs of being overweight and being obese according to birth weight. In the total population, the unadjusted OR for overweight in the high birth weight group (highest 25th percentile group) was 1.87 (95% CI 1.17-2.97) compared to the reference group. In the adjusted analysis, the high birth weight group also had higher risk of being overweight (aOR 1.75, 95% CI 1.11-2.76) compared to the reference group. In men, the unadjusted OR for being overweight was 2.32 (95% CI 1.30-4.16), and the association remained significant after adjustment of co-variates (aOR 2.19, 95% CI 1.20-3.98). However, there was no association between high birth weight and obesity in men (aOR 1.16, 95% CI 0.62-2.18). In contrast, in women, adjusted analysis demonstrated the association between high birth weight and being obese after adjustment (aOR 2.13, 95% CI 1.03-4.41), but no association with being overweight (aOR 1.05, 95% CI 0.47-2.37). After data imputation, results that were significant in the complete case analysis remained consistent. In the total population and male population, the high birth weight group had higher risk of being overweight (aOR 1.70, 95% CI 1.08-2.54; aOR

2.12, 95% CI 1.17-3.99) compared to the reference group after adjustment. In female population, high birth weight group had higher risk of being obese (aOR 2.18, 95% CI 1.11-4.49) compared to the reference group after adjustment.

Relationship between birth weight and body composition

The associations between birth weight, fat mass, and lean mass are presented in Figure 3 (total participants), Figure 4 (men), and Figure 5 (women). After adjusting for sociodemographic factors, the adjusted mean values of FMI increased significantly with increasing birth weight in the total population (P for trend: 0.03). However, LMI showed no significant increase with increasing birth weight (P for trend: 0.08). In male participants, higher birth weight was neither associated with higher FMI nor LMI (P for trend: 0.20, 0.25 respectively). In female participants, higher birth weight was associated with higher FMI (P for trend: 0.03), while LMI showed an inverse U-shape (P for trend: 0.25). Even after imputing the missing data, the overall trend of positive correlation between birth weight and FMI did not change. In women and the total population, FMI increased significantly with increasing birth weight (P for trend: <0.01 for both women and the total population). However, LMI did not increase with increasing birth weight (P for trend: 0.20).

Table 1. General characteristics of the study population

	Total (n=1,304)	Men (n=693)	Women (n=611)
Age (year), mean±s.d	14.7 (2.0)	14.7 (2.0)	14.8 (1.9)
Residence			
Capital	284 (21.8)	151 (21.8)	133 (21.8)
Metropolitan	279 (21.4)	148 (21.4)	131 (21.4)
Town/City	741 (56.8)	394 (56.9)	347 (56.8)
Household Income			
Lowest Third	144 (11.2)	64 (9.4)	80 (13.3)
Middle Third	727 (56.6)	385 (56.5)	342 (56.8)
Highest Third	413 (32.2)	233 (34.2)	180 (29.9)
Birth Weight, mean±s.d	3.3 (0.5)	3.3 (0.5)	3.2 (0.5)
Obesity			
Overweight ^a	162 (12.4)	97 (14.0)	65 (10.6)
General Obesity b	171 (13.1)	102 (14.7)	69 (11.3)
Body Composition			
Body Mass Index (kg/m ²), mean±s.d	21.0 (3.7)	21.2 (3.8)	20.7 (3.4)
Fat Mass Index (kg/m ²), mean±s.d	5.8 (2.5)	5.0 (2.5)	6.7 (2.2)
Lean Mass Index (kg/m ²), mean±s.d	15.0 (2.1)	16.0 (2.0)	13.8 (1.5)

Note: Data presented in number (percentage) with appropriate units unless otherwise stated.

^a Overweight: BMI ≥ 85 percentile BMI of age and sex or 23 kg/m², but not obesity

^b General Obesity (Korean criteria): BMI ≥ 95 percentile BMI of age and sex or 25 kg/m²

Table 2. Comparison of general characteristics between complete cases and cases with missing data

	Complete Case (n=884)	Missing Case ^c (n=206)	P value ^d	Missing Case e (n=420)	P value f
Age (year), mean±s.d	14.7 (1.9)	14.9 (2.0)	0.13	14.8 (2.0)	0.19
Residence			< 0.01		0.28
Capital	191 (21.6)	68 (33.0)		93 (22.1)	
Metropolitan	179 (20.3)	42 (20.4)		100 (23.8)	
Town/City	514 (58.1)	96 (46.6)		227 (54.1)	
Household Income			< 0.01		0.56
Lowest Third	103 (11.9)	54 (27.1)		41 (9.9)	
Middle Third	487 (56.1)	99 (49.8)		240 (57.7)	
Highest Third	278 (32.0)	46 (23.1)		135 (32.5)	
Birth Weight, mean±s.d	3.2 (0.5)	3.0 (0.8)	0.33	3.3 (0.5)	0.07
Obesity					
Overweight ^a	117 (13.2)	9 (10.3)	0.57	45 (10.7)	0.20
General Obesity b	114 (12.9)	10 (11.5)	0.66	57 (13.6)	0.74
Body Composition					
Body Mass Index (kg/m ²), mean±s.d	20.9 (3.6)	20.4 (3.5)	0.13	21.0 (3.7)	0.72
Fat Mass Index (kg/m ²), mean±s.d	5.8 (2.5)	5.3 (2.5)	0.15		
Lean Mass Index (kg/ m ²), mean±s.d	15.0 (2.1)	15.2 (2.3)	0.36		

Note: Data presented in number (percentage) with appropriate units unless otherwise stated.

^a Overweight: BMI ≥ 85 percentile BMI of age and sex or 23 kg/m², but not obesity

^b General Obesity (Korean criteria): BMI ≥ 95 percentile BMI of age and sex or 25 kg/m²

^c Cases with missing values on birth weight or BMI (cases removed from obesity analysis)

^d P value of the difference between complete case and missing case ^c

^e Cases with missing values on DXA (cases removed from body composition analysis)

^fP value of the difference between complete case and missing case ^e

Table 3: Crude and adjusted analyses of the association between birth weight and obesity in Korean adolescents

	Noncase ^a	Overweigh	t		General Ob	esity	
Birth Weight	Weighted	Weighted	Crude OR	Adjusted ^b OR	Weighted	Crude OR	Adjusted ^b OR
-	Proportion	Proportion	(95% CI)	(95% CI)	Proportion	(95% CI)	(95% CI)
	%	%			%		
Men (n=693)							
0-25 % (n=141)	70.1	14.9	1.54 (0.76-3.12)	1.46 (0.70-3.05)	15.0	1.13 (0.57-2.24)	1.09 (0.55-2.16)
25-75 % (n=354)	75.3	10.4	1 (referent)	1 (referent)	14.3	1 (referent)	1 (referent)
75-100 % (n=198)	65.3	21.0	2.32 (1.30-4.16)	2.19 (1.20-3.98)	13.7	1.11 (0.62-2.00)	1.16 (0.62-2.18)
P for trend			0.17	0.19		1.00	0.83
Women (n=611)							
0-25 % (n=163)	81.7	8.2	0.79 (0.37-1.69)	0.80 (0.38-1.69)	10.0	0.89 (0.43-1.84)	0.95 (0.46-1.97)
25-75 % (n=326)	79.0	10.1	1 (referent)	1 (referent)	10.9	1 (referent)	1 (referent)
75-100% (n=122)	71.7	9.2	1.01 (0.47-2.15)	1.05 (0.47-2.37)	19.1	1.92 (0.93-3.96)	2.13 (1.03-4.41)
P for trend			0.55	0.52		0.08	0.08
Total (n=1,304)							
0-25 % (n=304)	76.4	11.3	1.11 (0.66-1.87)	1.15 (0.67-1.96)	12.3	0.98 (0.59-1.61)	1.05 (0.63-1.74)
25-75 % (n=680)	77.1	10.3	1 (referent)	1 (referent)	12.7	1 (referent)	1 (referent)
75-100% (n=320)	67.6	16.8	1.87 (1.17-2.97)	1.75 (1.11-2.76)	15.6	1.40 (0.89-2.21)	1.51 (0.95-2.42)
P for trend			0.08	0.14		0.19	0.20

Acronyms: OR, Odds Ratio; CI, Confidence Intervals

^a Those being neither overweight nor obese.

b Adjusted for age, sex, residence, and household income.

DISCUSSION

In this cross-sectional study of Korean adolescents, we have shown that higher birth weight was associated with a higher risk of being overweight in men and obese in women. Also, higher birth weight was associated with greater BMI and FMI, but not LMI.

Higher birth weight was associated with increased risk of being overweight in the total population and in male adolescents. This is consistent with previous cohort studies that showed birth weight is associated with being overweight in male adolescents[11,20]. Furthermore, high birth weight was associated with increased risk of obesity among women, but not in men or the total population. This differs from previous studies that have shown that high birth weight increased the risk of obesity in adolescents in both men and women[8,10]. However, it was consistent with another study[11] that additionally adjusted for family income. Several other studies have shown that higher birth weight is associated with being overweight or obese in children[8,21], and in adults[5,22,23]. It is known that alterations in body fat distribution begin during puberty due to hormones including cortisol, insulin, growth hormone, and sex steroids[24]. The fact that adolescents are physiologically different in body composition from children and adults may account for the differing results from studies that targeted children or adults.

Higher birth weight was related to higher FMI, but not LMI. This contradicts preceding studies which have shown that higher birth weight is associated with greater lean mass[12-14]. One possible explanation for this trend in increasing fat mass but not lean mass with greater birth weight may be due to the fact that Asians tended to have greater proportions of fat compared to other ethnicities. It has been shown that BMI and body fat percent are ethnic specific, possibly due to the differences in frame size, relative leg length and physical activity level[15,16,25].

The linear relationship between birth weight and FMI contradicts some of the previous studies that have shown J- or U-shaped relationships between birth weight and fat mass[8,26,27]. Previous studies have attempted to explain the J- or U-shaped relationship between birth weight and fat mass by citing studies that show infants who are born small experience rapid catch up growth in early infancy, which results in larger fat mass in later life[28,29]. While we could not reveal clear reasons for the discrepancy in our results compared to previous studies as we did not have information on postnatal weight gain, one possible explanation may be due to the ethnic differences of body composition as mentioned previously. Future studies investigating the association between birth weight and postnatal weight gain in terms of the effect of body composition are needed.

The significant association between birth weight, obesity, and FMI may be explained by genetic factors. It is said that about 50% of the variance in birth weight and more than 50% of the variance in BMI are attributed to shared genetic factors[30,31]. Therefore, it seems rational to speculate that the genetic factors that made infants heavier could also contribute to the increased risk of greater BMI later in life. Another explanation could be that intrauterine environment, which contributes to birth weight, also affects the formation of the fetal organs involved in energy metabolism by altering the transfer of metabolic substances between mother and fetus[32].

In this study, the relationship between birth weight and both obesity and body composition was different among men and women. Similarly, among previous studies that dealt with relationships between birth weight and possible outcomes in later life including obesity, blood pressure[33], lipid levels[34] and insulin action[35], many have shown gender differences. As those factors, such as metabolic variables and blood pressure, are closely related to body composition[36-38], these findings indicate that men and women could have different mechanisms for body composition. It is suggested that sex steroid hormones alter the body composition during pubertal development[39,40]. Estrogen, for example, is known to play a crucial role in body fat distribution[39]. This difference in hormone actions lead to more increased lean mass in boys, and comparatively high fat mass in girls[41]. Moreover, some studies suggested that bone and muscle growth may be programmed differently by gender during intrauterine life[42,43]. These factors may have contributed to the strong association between birth weight and FMI in women.

There are several limitations in this study. First, since observational data was used, inferences about causal effects cannot be made clearly and only assumptions about the relationship can be suggested. Further studies are needed to clarify the causality and its mechanism. Secondly, birth weight was self-reported in a survey, which means that the data could be less accurate compared to birth records. Although parental factors including maternal obesity, diabetes may influence the birth weight of their offspring, such information are not included in this survey. Despite these limitations, we tried to account for parental factors by adjusting for household income. Also, we used a large study population (n=1,304) and performed sensitivity analysis, which makes our study generalisable to the Korean population, while further studies on other population are recommended to apply the results to other ethnics. Most importantly, this study targeted Koreans, an ethnicity few previous studies have investigated upon, suggesting that ethnic differences and gender differences may exist in the body composition and in the risk of developing obesity.

CONCLUSION

The results of our study suggest that high birth weight may be an indicator of being overweight in Korean adolescents. Particularly in women, high birth weight is associated with higher risk of general obesity. High birth weight was associated with greater fat mass compared to lean mass. These findings suggest that those born with high birth weight, may be more susceptible to being overweight and obese and may merit close monitoring and early intervention against obesity.



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CONTRIBUTORSHIP

In this study, Myunggee Kang designed the study, analysed the data, interpreted the results and wrote the paper as a first author. Jung Eun Yoo and Seulggie Choi contributed to data analysis and result interpretation. Kyuwoong Kim contributed to data analysis and literature research. Sang Min Park contributed to study design and results interpretation. All authors were involved in revising the paper and approved the final paper as submitted.

CONFLICT OF INTEREST STATEMENT

No conflict of interest was declared.

ETHICAL APPROVAL

This study did not need ethical approval of our Institutional Review Board, since the survey data examined were publicly available.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or notfor-profit sectors

DATA SHARING

All relevant materials are provided in the manuscript. KNHANES V, raw data used in this is available from http://knhanes.cdc.go.kr.

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- Figure 1: Flow Diagram of the Selection Procedure for the Study Population
- **Figure 2:** Least-squares means of BMI in total participants (n=1304), male (n=693), and female (n=611). We adjusted for age, sex, residence and household income according to birth weight.
- **Figure 3:** Least-squares means of FMI and LMI in total participants (n=884). We adjusted for age, sex, residence and household income according to birth weight.
- **Figure 4:** Least-squares means of FMI and LMI in male participants (n=407). We adjusted for age, sex, residence and household income according to birth weight.
- **Figure 5:** Least-squares means of FMI and LMI in female participants (n=477). We adjusted for age, sex, residence and household income according to birth weight.

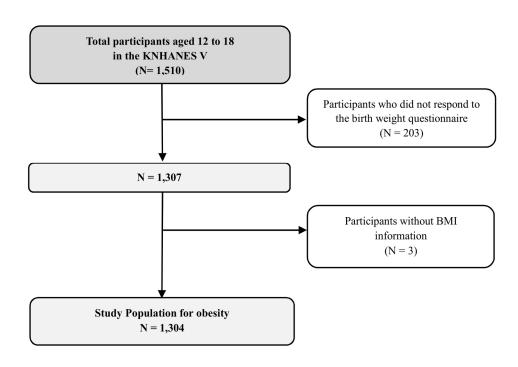


Figure 1: Flow Diagram of the Selection Procedure for the Study Population $87x59mm (600 \times 600 DPI)$

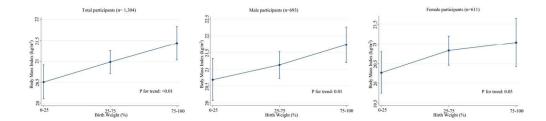


Figure 2: Least-squares means of BMI in total participants (n=1304), male (n=693), and female (n=611). We adjusted for age, sex, residence, and household income according to birth weight.

57×13mm (600 × 600 DPI)

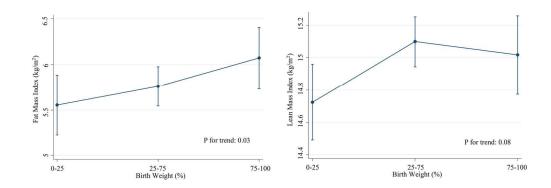


Figure 3: Least-squares means of FMI and LMI in total participants (n=884). We adjusted for age, sex, residence, and household income according to birth weight.



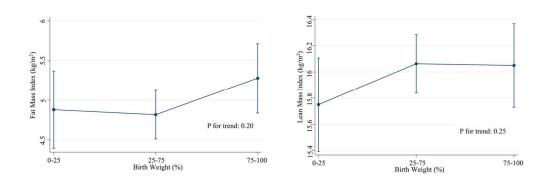


Figure 4: Least-squares means of FMI and LMI in male participants (n=407). We adjusted for age, sex, residence, and household income according to birth weight.



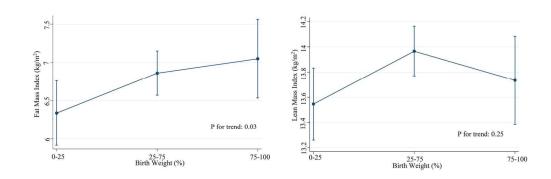


Figure 5: Least-squares means of FMI and LMI in female participants (n=477). We adjusted for age, sex, residence and household income according to birth weight.



STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	5,6
		(d) If applicable, describe analytical methods taking account of sampling strategy	6
		(e) Describe any sensitivity analyses	6
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	5
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8
		(b) Indicate number of participants with missing data for each variable of interest	7
Outcome data	15*	Report numbers of outcome events or summary measures	7,8,9
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(b) Report category boundaries when continuous variables were categorized	5,6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7,8
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12,13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.